Botulinum Toxin Injection Therapy
Paediatric Movement Disorder Service
Full Clinical Guideline – Derby only

Reference no.: CH CLIN G 134/May 21/v002

1. Introduction

Children and young people with Cerebral Palsy and acquired brain injury can have muscle stiffness and involuntary muscle over-activity, mostly referred to as spasticity. Children and young people with spasticity tend to develop harmful effects such as pain, altered motor patterns, deformity and impaired function. These children are seen in the paediatric movement disorder service (PMDS) and are planned for Botulinum Toxin injection therapy. The local intramuscular injection of Botulinum Toxin is an established, well tolerated treatment in the management of focal spasticity.

In the UK, for children and young people, Botulinum Toxin is licensed for treatment in the calf muscles. It has also become an accepted part of routine management in other muscle groups of the lower and upper limbs. Therefore, the selection of appropriate patients and the definition of clear, achievable, realistic and measurable goals are crucial to the successfully administering Botulinum Toxin injection therapy (Papavasiliou et al., 2013).

2. Aim and Purpose

This guideline is aimed at providing the Botulinum toxin injectors, nurses, play therapists, healthcare assistants and other professionals with adequate information, knowledge and understanding. The guideline also aims to provide the tools to manage and support the Botulinum Toxin injection clinics at the Derbyshire Children's Hospital in a safe and clinically effective manner.

The purpose of the document is to ensure that the practitioners involved in the clinics follow the latest and best practice guidelines as proposed by the National Institute for Clinical Excellence (NICE, 2012), National clinical safety organisations and agreed consensus documents.

3. Definitions, Keywords

Cerebral Palsy (CP), describes a group of permanent disorders of movement and posture causing activity limitation that are attributed to non-progressive disturbances that occurred in the developing foetal or infant brain. The motor disorders of cerebral palsy are often accompanied by disturbances of sensation, perception, cognition, communication and behaviour, by epilepsy, and by secondary musculoskeletal disorders'. (Rosenbaum P et al: Dev Med Child Neurol (Suppl.) 2007;109:8-14)

Botulinum toxin - Type A (BTX-A), commonly referred to as Botox is a neurotoxin that is produced from bacteria called Clostridium Botulinum under laboratory conditions.

Spasticity, an involuntary muscle over-activity commonly occurs when there is damage to the central nervous system (brain and spinal cord). It presents in a variety of ways with varying levels of severity depending on the size, location and nature of the lesion.

4. Botulinum Toxin Injection Therapy

a. Indications and Patient selection

As BTX-A reduces over-activity in spastic or dystonic muscles, successful outcome is dependent on identifying the appropriate goals and accurate selection of the muscles that are primarily responsible for the identified problem. Therefore, in children and young people, BTX-A is considered for the following problems noticed in the upper and lower limbs,

- Impeding gross and fine motor function
- Compromising care and hygiene
- Causing pain
- Disturbing sleep
- Impeding tolerance of other treatments such as orthoses and use of equipment to support posture
- Causing cosmetic concerns to the child or young person

A trial of BTX-A is considered in children and young people with spasticity in whom focal dystonia is causing serious problems, such as postural, or functional difficulties or pain. Although licensed only for use in Cerebral Palsy, BTX-A may also be appropriate for children with,

- Post traumatic brain injury
- Genetic conditions (hereditary spastic paraplegia)
- Metabolic conditions
- Neurodegenerative disorders

Generally, in the Paediatric Movement Disorder Service, a child or a young person is considered for BTX-A treatment when there is focal/dynamic spasticity, and/or dystonia which may now or in the future interfere with function, care-giving resulting in secondary disorders such as torsional abnormalities or cause pain.

b. Model of action

BTX-A is a local muscle relaxant that is highly selective for peripheral nerve terminals acetylcholine. When injected into the muscle, the toxin is taken up into the nerve terminal by endocytosis. Once inside the nerve cell, BTX-A prevents the release of acetylcholine into the synaptic cleft resulting in a reduced muscle contraction. BTX-A is taken up by the neuromuscular junction within 12 hours. The onset however varies, but usually occurs gradually over the first week. There can be huge variation in clinical response with some effects observed immediately or in some cases after 2-3 weeks. The effects of the injection is temporary with recovery of the nerve terminal taking place via sprouting, gradually over 12 – 16 weeks. Although the clinical response varies, generally the injected muscles show some weakness for 3-4 months. In some cases, the functional benefits of BTX-A may continue long after the chemical effects of the BTX-A have gone. Due to temporary effects of BTX-A, repeat injections may be required.

c. Management of Botulinum Toxin injection clinics and it administration

Children and young people receive injections with the use of one of more of the following interventions to reduce pain, anxiety or distress children are either admitted to paediatric day case for injections, or injections are administered in theatre if under general anaesthetic.

Children receiving injections will receive pain relief under one of the following methods:

- General anaesthesia
- Oral sedation such as Midazolam
- Nitrous oxide (Entonox gas)
- No sedation, Ethyl chloride or topical anaesthetics over the injection sites

If the child/young person is planned for injections under Midazolam or Nitrous oxide sedation or with just ethyl chloride, they are admitted to the day case ward at the Derbyshire Children's Hospital.

Following is the practice guidelines / step-by-step guide for managers, practitioners and support staff who are involved in the management of the children with Botulinum Toxin injections.

Preparations and protocols before the injection

4.3.1 Ensure that the practitioners and the support staff have a thorough understanding of the procedures and the protocols to be followed for the clinics

4.3.2 The designated nurse in charge of the Botulinum injection clinic ensures that the Botulinum injections are received from the pharmacy and are stored in the refrigerator in the ward. Also ensure that the notes and the prescription sheets are made available for the clinic

4.3.3 Before the start of the clinic, ensure that the ultrasound scanner (kept in Children's Emergency Department) is available for the clinic. Along with it, prepare the Botulinum Toxin injection trolley with the equipment listed in appendix 1.

4.3.4 The child / young person and family should be advised to arrive 30 – 60 minutes prior to the procedure. When they arrive on the ward, they are introduced to the lay out of the ward and the proposed procedure explained

4.3.5 The child / young person is weighed and staff check if they are within 10% of the previous weight (as shown in the prescription sheet). If it is under or over the 10% margin, medication may need to be altered, therefore this should be discussed with the Consultant/Physiotherapy Practitioner

4.3.6 Parents and family members stay with the child / young person throughout their stay at the ward. Allow the child / young person to play in the play area until they have had sedation

4.3.7 The play therapist designated for Botulinum toxin clinics is introduced to the child / young person and the family, and supports them through the procedure

4.3.8 The clinician who will be injecting the Botulinum toxin meets with the child / young person and the family and checks with the family to ensure that the child is in good health to receive the injections. Then the clinician confirms the proposed injection plan and explains the procedure. A written, signed consent should be obtained from the person with the parental responsibility

on the day of injection, at this stage the risks and benefits of treatment should be discussed and documented on a trust consent form.

4.3.9 The clinician who will be injecting the Botulinum toxin ensures that the injection sites are indicated by clearly marking all the sites of injection. When only one side of the limb is planned for injections, indicate the side with a permanent black marker. If multiple injection sites have been identified, ensure that the sides of the limbs are marked clearly

4.3.10 If topical anesthetics/numbing cream is indicated for numbing the skin overlying the muscles to be injected, the designated nurse checks with the parent regarding any allergic reaction and applies the cream evenly on the belly of the muscle to be injected. The numbing cream needs to be covered with cling film or other suitable covering. The exact time of application of the cream should be documented on the prescription sheet

4.3.11 Following this, sedation and pain relief should be administered as per prescription. The designated nurse needs to check the dosage with an appropriate colleague (follow the ward protocols). The time of administering the sedation and pain relief medication should be documented

4.3.12 Occupy the child / young person with play therapy until sedation begins to take effect. For the sedation to work effectively, ensure that the child can relax and the area is conducive for calming and relaxing

Protocols and procedures during the injection

4.4.1 The nurse prepares the clinic room: ultrasound machine is kept ready along with the injection trolley (check separate documentation for preparation of the trolley). The designated nurse brings the Botulinum injection pack from the refrigerator and keeps it ready in the clinic room

4.4.2 The clinician checks Botulinum toxin vial, expiry date and the dosage with the nurse allocated to the botulinum clinic that day and prepares the injections

4.4.3 The child/ young person is brought to the injection room with their family member and the play therapist

4.4.4 The clinician briefs the nurse, play therapist and the family member, (child/young person if applicable) about the plan i.e. sequence of the injections, positioning and turning protocols

4.4.5 The child is supported appropriately by the team with suitable forms of distraction. If the muscle wrap film/cling film was applied, it can now be removed as applicable.

4.4.6 If the child is planned to have Entonox gas, the nurse (Entonox trained) administers Entonox with the support of a colleague (Nurse/HCA)

4.4.7 The muscles to be injected are localized using one of the following methods: ultrasound/electrical stimulator/electromyography. Ultrasonography allows non-invasive, real-time imaging of muscular and soft tissues and their surrounding structures (Walter, 2014). The precise identification of the muscles to be injected is critical to the intended outcomes. Therefore, the clinician chooses to use one of the above methods by taking into account the following factors: type and location of the muscle, established clinical practice along with the clinician's experience in using the procedure

4.4.8 Following injections, the child/young person will be reviewed by the clinician in the outpatient clinic to evaluate the outcomes of the injections. Depending

on the individual clinical indication, this review is carried out between 1 and 3 months, or between 3 and 6 months. Further to this review, the clinician plans to continue with further course of management. This might involve continuing with further Botulinum toxin injections or refer the child/young person to other relevant clinicians. For further information, refer to the parent information leaflet: Paediatric Movement Disorder Clinics

5. Injection dosage – safety profile

During the initial and review assessments, the clinician administers a range of clinical assessments, and gathers both subjective and objective information. This information is used to both identify the appropriate muscles for injection, as well as choose the required effective dose for each of those muscles. Following each post injection review, the administered dosage is continuously evaluated and adjusted to achieve the planned outcomes, whilst ensuring safe dosage limits (Bakheit et al., 2001). The dosage choice for the multi-level Botulinum toxin injection therapy should be guided by the following characteristics.

Long-term applicability, sustainability, individual and flexible planning,

5.1.1 Abobotulinum toxin A (Dysport): Start with dosage of ≤20 units/kg body weight for the first injection and subsequent injections of ≤30 units/kg body weight with a maximum total dose of 1000 units abobotulinum toxin A (Strobl etal., 2015). Refer to Appendix 3

5.1.2 Onabotulinum toxin A (Botox): Start with ≤12 units/kg body weight for the first injection and subsequent injections ≤15 units/kg body weight with a maximum total dose of 300 units onabotulinum toxin A, following conservative recommendations (Strobl et al., 2015)

5.1.3 Individualisation of the dosage is critical, with early initiation of injection therapy, medium-dose, multi-level injections are indicated, supporting long-term and sustainable intervention

5.1.4 The safety profile of the recommended doses of Botulinum toxin A is the same for children under two years as for older children (Strobl et al., 2015)

6. Adverse events management protocol

a. Adverse reactions/effects following Botulinum toxin injections

6.1.1 The use of Botulinum toxin in the management of spasticity has been proven to be safe and effective (Papavasiliou, 2013). Adverse events attributed to the systemic spread of the toxin are uncommon and include flu like symptoms and generalised weakness. Rarely children may experience breathing or swallowing difficulties and parents should be advised to seek urgent medical attention should this occur

6.1.2 Some of the specific adverse reactions noticed in children having Botulinum toxin injections include myalgia, muscular weakness, urinary incontinence, influenza-like illness, injection site reaction (e.g. pain, erythema, brusing etc.), gait disturbance, fatigue and injection site rash

6.1.3 Children and young people with cerebral palsy can be categorized into 5 different levels using a tool called gross motor function classification system

(GMFCS). GMFCS looks at movements such as sitting, walking and the use of mobility devices to classify the children from level I to V. This helps the families and the clinicians to use standardised descriptions and have a clear understanding of the child/young person's current motor function. Children and young people classified under GMFCS levels IV & V have a higher chance of experiencing adverse effects than children under GMFCS levels I to III (Strobl et al., 2015). Therefore, the clinician exercises caution when treating these children

6.2 Overdose

6.2.1 Excessive doses may produce distant and profound neuromuscular paralysis. Overdose could lead to an increased risk of the neurotoxin entering the blood stream and may cause complications associated with the effects of oral botulinum poisoning (e g. Dysphagia and Dysphonia). Respiratory support may be required where excessive doses cause paralysis of respiratory muscles. General supportive care is advised. In the event of overdose, the patient should be medically monitored for signs and/or symptoms of excessive muscle weakness or muscle paralysis. Symptomatic treatment should be instigated if necessary.

6.3 Adverse incident – management and reporting

6.3.1 The clinician ensures the safety of the child/young person and the family; explains to the child and the family about the incident, the risks associated with the incident and the management plan. The child and the family are provided with adequate information if further support is needed

6.3.2 The clinician ensures that the incident is documented in the child/young person's notes; discusses the risks and the management plan with the child's consultant

6.3.3 The incident is recorded in the hospital DATIX reporting system and the cause of the incident is explored and discussed for avoiding such incidents in the future

7. References

7.1. Strobl, W., Theologis, T., Brunner, R., Kocer, S., Viehweger, E., Pascual-Pascual, I., Placzek, R. 2015. Best clinical practice in botulinum toxin treatment for children with cerebral palsy. Toxins, 7, 1629-48

7.2. NICE Clinical Guidelines 2012: Spasticity in children and young people with non-progressive brain disorders: Management of spasticity and co-existing motor disorders and their early musculoskeletal complications

7.3. Peter Rosenbaum et al The Definition and Classification of Cerebral Palsy *Developmental Medicine & Child Neurology2007 supplement Dev Med Child Neurol Suppl* 2007; 109: 8–14

7.4. Richards RN. Ethyl chloride spray for sensory relief for Botulinum toxin injections of the hands and feet. Journal of cutaneous medicine and surgery, 2009, Sep-Oct, 13(5), 253-56

7.5. Papavasiliou, A.S., Nikaina, I., Filiopoulos. 2013. Safety of Botulinum Toxin A in children and Adolescents with Cerebral Palsy in a Pragmatic setting. Toxins (Basel). 5(3): 524-53

7.6. Wang, Y., Gao, B. 2008. A dose-response relationship research on botulinum toxin type a local intramuscular injections of lower extremity spasticity in children with cerebral palsy. Child's Nervous Syst. ChNS: Off. J. Int. Soc. Pediatr. Neurosurg, 24, 545–547

7.7. Wohlfarth, K., Muller, C., Sassin, I., Comes, G., Grafe, S. 2007. Neurophysiological double-blind trial of a botulinum neurotoxin type a free of complexing proteins. Clin. Neuropharmacol, 30, 86–94

7.8. Wissel, J.; Heinen, F.; Schenkel, A.; Doll, B.; Ebersbach, G.; Muller, J.; Poewe, W. Botulinum toxin a in the management of spastic gait disorders in children and young adults with cerebral palsy: A randomized, double-blind study of "high-dose" versus "low-dose" treatment. Neuropediatrics 1999, 30, 120–124

7.9. Kanovsky, P.; Bares, M.; Severa, S.; Richardson, A.; Dysport Paediatric Limb Spasticity Study Group. Long-term efficacy and tolerability of 4-monthly versus yearly botulinum toxin type a treatment for lower-limb spasticity in children with cerebral palsy. Dev. Med. Child Neurol. 2009, 51, 436–445

7.10. Gough, M.; Fairhurst, C.; Shortland, A.P. Botulinum toxin and cerebral palsy: Time for reflection? Dev. Med. Child Neurol. 2005, 47, 709–712

7.11. Walter, U., Dressler, D. 2014. Ultrasound-guided botulinum toxin injections in neurology: technique, indications and future perspectives. 14(8):923-36

7.12. Bakheit, A.M.O., Severa, S., Cosgrove, A., Morton, R., Roussounis, S.H., Doderlein, L., Lin, J-P. 2001. Safety profile and efficacy of botulinum toxin A (Dysport) in children with muscle spasticity. Developmental medicine and child neurology

7.13. Canchild. 2017. [Accessed Online]. https://www.canchild.ca

7.14. Datapharm, 2021, https://www.medicines.org.uk/emc/product/7261/smpc [accessed on 8th Jan 2021]

8. Documentation Controls

<table>
<tr><td>Reference Number

CH CLIN G 134/May 21/v002</td><td colspan="2">Version: 2</td><td>Status

Final</td><td></td></tr>
<tr><td rowspan="2">Version / Amendment History</td><td>Version</td><td>Date</td><td>Author</td><td colspan="2">Reason</td></tr>
<tr><td>2</td><td>May 2024</td><td>Mr. Saran Muthiah</td><td colspan="2">Guideline required renewal</td></tr>
<tr><td colspan="6">Intended Recipients: Clinical and Administrative staff (stakeholders) involved in the delivery and management of Paediatric Movement Disorder Service (PMDS)</td></tr>
<tr><td colspan="6">Training and Dissemination: One-to-one session, Training Sessions, Workshops</td></tr>
<tr><td colspan="6">Development of Guideline: Mr. Saran Muthiah
Job Title: Extended Scope Physiotherapy Practitioner</td></tr>
<tr><td colspan="6">Consultation with: Dr. R Bowker</td></tr>
<tr><td colspan="6">Linked Documents: None</td></tr>
<tr><td colspan="6">Keywords: Botulinum Toxin (Botox), Cerebral Palsy, Muscle Relaxant, Spasticity</td></tr>
<tr><td colspan="3">Business Unit Sign Off</td><td colspan="3">Group: Paediatric Guidelines Group
Date: 5th May 2021</td></tr>
<tr><td colspan="3">Divisional Sign Off</td><td colspan="3">Group: Women’s and Children’s Clinical Governance
Date: 25th May 2021</td></tr>
<tr><td colspan="3">Date of Upload</td><td colspan="3">11/06/2021</td></tr>
<tr><td colspan="3">Review Date</td><td colspan="3">May 2024</td></tr>
<tr><td colspan="3">Contact for Review</td><td colspan="3">Saran Muthiah</td></tr>
</table>

9. Appendices

Appendix 1: Botulinum Toxin trolley List
Appendix 2: Physiological development/motor milestones
Appendix 3: Dysport maximum total doses per treatment session and minimum times before treatment

Appendix 1

<u>Equipment required for Botulinum Toxin injection Trolley</u>

1. *Ultrasound scanner located in CED*
2. *Ultrasound gel*
3. *Syringes – 1ml, 2 ml, 5 ml*
4. *Needles – 27g/2 inches, 19g/2 inches*
5. *0.9% sodium chloride*
6. *Plasters*
7. *Sterets*
8. *Gauze*
9. *Ametop cream*
10. *Cold spary*
11. *Yellow striped bags for waste*
12. *Sharps box*
13. *Marker Pens*
14. *Sterile trays*
15. *Entonox gas*
16. *Botulinum toxin injections*
17. *Water for injection*

Appendix 2

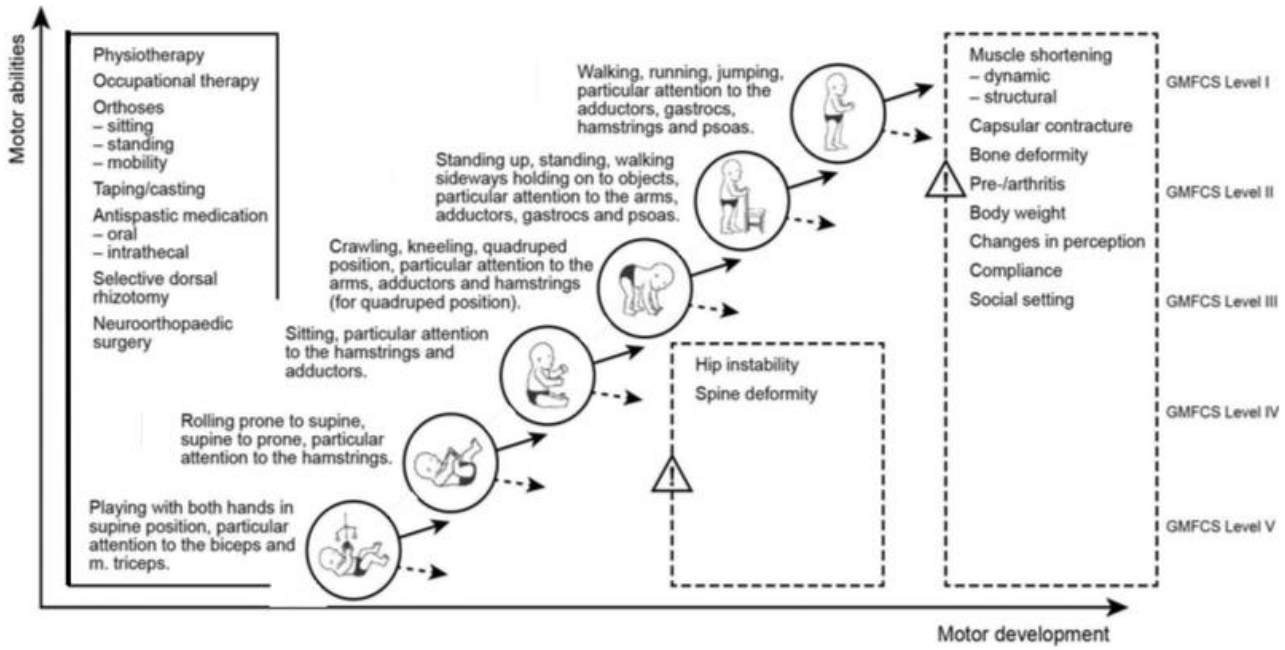

Image from Strobl et al., 2015, showing

Physiological development/motor milestones with available therapy options listed in the left box. To every milestone, the affected muscles (key muscles for Botulinum toxin injection) are displayed. In case of stagnation (dashed arrows), secondary alterations and deformities are shown in the right box.

Appendix 3

Dysport maximum total doses per treatment session and minimum times before retreatment

Limb	Maximum total dose of Dysport to be administered per treatment session	Minimum time before retreatment should be considered
Single lower limb Both lower limbs	15 units/kg or 1000 units* 30 units/kg or 1000 units*	No sooner than 12 weeks
Single upper limb Both upper limbs	16 units/kg or 640 units* 21 units/kg or 840 units *	No sooner than 16 weeks
Upper and lower limbs	30 units/kg or 1000 units*	No sooner than 12-16 weeks

*whichever is lower

Table from Datapharm, 2021, https://www.medicines.org.uk/emc/product/7261/smpc
[accessed on 8th Jan 2021]